UNIVERSITY OF TECHNOLOGY SYDNEY

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# APPLICATION OF ADVANCED NEURAL NETWORKS IN HYPOGLYCEMIA DETECTION SYSTEM

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(*B.Eng.* & *M.Sc.* & *M.Eng.*)

THIS THESIS IS SUBMITTED

FOR THE REQUIREMENT OF DOCTOR OF PHILOSOPHY TO

FACULTY OF ENGINEERING & INFORMATION TECHNOLOGY

UNIVERSITY OF TECHNOLOGY, SYDNEY

APRIL 2013

# Acknowledgments

First of all, I would like to express my appreciation to my supervisor, Dr. Steve Ling for his continuous advice, insightful discussions and remarks on many occasions that are extremely helpful in improving my research work as well as my thesis.

I am also very grateful to my co-supervisor, Professor Hung Tan Nguyen for his valuable suggestions, thoughtful guidance and support throughout my PhD studies.

My special thanks to all colleagues and staff members in the Center for Health Technology, University of Technology, Sydney. I also place on record my sense of gratitude to one and all who directly or indirectly having lent me a helping hand during my studies.

Latest but not least, I wish to express my love and gratitude to my parents, Mr. Pe Than and Mrs. Khin Win Yee for their unceasing encouragement and continuous support in various ways. Deepest appreciation to my husband, Mr. Wunna Tun and my son, Nyi Lin San for their understanding and continuous support through the duration of my studies.

# Certificate of Authorship/Originality

I hereby declare that this thesis is my own work and effort and that it has not been submitted anywhere for any award. Any help that I have received in my research work and the preparation of the thesis itself has been acknowledged.

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# Abstract

Hypoglycemia is the medical term for a state produced by lower levels of blood glucose. It represents a significant hazard in patients with Type 1 diabetes mellitus (T1DM) which is a chronic medical condition that occurs when the pancreas produces very little or no insulin. The imperfect insulin replacement places patients with T1DM at increased risk for frequent hypoglycemia. Deficient glucose counter-regulation in T1DM patients may even lead to severe hypoglycaemia even with modest insulin elevations. It is very dangerous and can even lead to neurological damage or death. Thus, continuous monitoring of hypoglycemic episodes is important in order to avoid major health complications.

Conventionally, the detection of hypoglycemia is performed by puncturing the fingertip of patients and estimate the blood glucose level (BGL) as well as the stage of hypoglycemia. However, the direct monitoring of BGL by extracting blood sample is inconvenient and uncomfortable, a more appealing preposition for preventing hypoglycemia is to monitor changes in relevant physiological parameters. Findings from numerous studies indicate that sudden nocturnal death in type 1 diabetes is thought to be due to ECG QT prolongation with subsequent ventricular tachyarrhythmia in response to nocturnal hypoglycaemia. Though several parameters can be monitored, the most common physiological parameters to be effected from a hypoglycemic reaction are heart rate (HR) and corrected QT interval (QTc) of the ECG signal. Considering the real-time physiological parameters (HR and QTc) changes during hypoglycemia, a non-invasive monitoring of glycemic level is predicted for the hypoglycemia.

The topic of this thesis is covered by novel methodologies for the non-invasive hypoglycemia detection system by analyzing the behavioral changes of physiological parameters such as HR and QTc. These algorithms are comprised of three different classification techniques, i) variable translation wavelet neural network (VTWNN), ii) multiple regression-based combinational neural logic network (MR-NLN) and iii) rough-block-based neural network (R-BBNN). By taking the advantages of these proposed network structures, the performance in terms of sensitivity and specificity of non-invasive hypoglycemia monitoring system is improved.

The first proposed algorithm is VTWNN in which the wavelets are used as transfer functions in the hidden layer of the network. The network parameters, such as the translation parameters of the wavelets are variable depending on the network inputs. Due to the variable translation parameters, the proposed VTWNN has the ability to model the inputoutput function with input-dependent network parameters. Effectively, it is an adaptive network capable of handling different input patterns and exhibits a better performance. With the adaptive nature, the network provides a better performance and increases the learning ability. For conventional wavelet neural network, a fixed set of weight is offered after the training process and fail to capture nonstationary nature of ECG signal. To overcome with this problem, VTWNN with multiscale wavelet function is firstly introduced in this thesis. With the variable translation parameter, the proposed VTWNN gives faster learning ability with better generalization.

The second algorithm, MR-NLN is systematically designed which is based on the characteristics of application. Its design is based on the binary logic gates (AND, OR and NOT) in which the truth table and K-map are constructed and it depends on the knowledge of application. Because the logic theory are used in the network design, the structure becomes systematic and simpler compared to other conventional neural networks (NNs) and enhance the training performance. Traditionally, the conventional NNs with the same structure are applied to handle different applications. The optimal performance may not always guaranteed due to different characteristics of applications. In real-world applications, the knowledge based-neural network that understands all the characteristics of practical applications are preferred for optimal performance. In conventional NNs, the redundant connections and weights of conventional neural networks make the number of network parameters unnecessarily large and downgrades the training performance. But for neural logic network (NLN), the structure becomes simpler.

The third algorithm focuses on the hybridization technology using rough sets concepts and neural computing for decision and classification purposes. Based on the rough set properties, the input signal is partitioned to a predictable (certain) part and random (uncertain) part. In this way, the selected block-based neural network (BBNN) is designed to deal only with the boundary region which mainly consists of a random part of applied input signal and caused inaccurate modeling of data set. Due to the rough set properties and the adaptability of BBNN's flexible structures in dynamic environments, the classification performance is improved. Owing to different characteristics of neural network (NN) applications, a conventional neural network with a common structure may not be able to handle every applications. Based on the knowledge of application, BBNN is selected as a suitable classifier due to its modular characteristics and ability in evolving the size and structure of the network.

To obtain the optimal set of proposed network parameters, a global learning optimization algorithm called hybrid particle swarm optimization with wavelet mutation (HPSOWM) is introduced in this thesis. Compared to other stochastic optimization methods, the hybrid HPSOWM has comparable or even superior search performance for some hard optimization problems with faster and more stable convergence rates. During the training process, a fitness function which is characterized by the proposed network design parameters is optimized by reproducing a better fitness value.

The proposed systems is validated using clinical trial conducted at the Princess Margaret Hospital for Children in Perth, Western Australia, Australia. A total of 15 children with 529 data points (ages between 14.6 to 16.6 years) with Type 1 diabetes volunteered for the 10-hour overnight for natural occurrence of nocturnal hypoglycemia. Prior to the application of the algorithms, the correlation between the measured physiological parameters, HR and QTc and the actual BGL for each subject were analyzed. The feature extracted ECG parameters, HR and QTc significantly increased under hypoglycemic conditions ($BGL \leq 3.3 mmol/l$) according to their respective $p$ values, HR ($p < 0.06$) and QTc ($p < 0.001$). The observation on these changes within the physiological parameters have provided the groundwork for model classification algorithms.

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# List of Symbols and Abbreviations

| | |
|---|---|
| $a$ | Dilation parameter of multi-wavelet |
| $b$ | Translation parameter of multi-wavelet |
| $n_{in}$ | Number of network inputs |
| $n_h$ | Number of hidden nodes |
| $n_{out}$ | Number of network outputs |
| $\psi_{a,b}(\cdot)$ | Multi scaled wavelet function |
| $\psi(\cdot)$ | Mother wavelet function |
| $n_{para}$ | Total number of network parameters |
| $para_{\max}^{j}$ | Maximum value (Upper boundary) of particle element |
| $para_{\min}^{j}$ | Minimum value (Lower boundary) of particle element |
| $v_{\max}$ | Maximum velocity of particle |
| $v_{\min}$ | Minimum velocity of particle |
| $f(\cdot)$ | Activation function |
| $u_i$ | Input variables |
| $v_{ij}$ | Weight between $i$th input and $j$th hidden nodes |
| $w_{jl}$ | Weight between $j$th hidden and $l$th output nodes |
| $b_j$, $b_l$ | Biases for hidden and output nodes |
| $logsig(\cdot)$ | Logarithmic sigmoid transfer function |
| $tansig(\cdot)$ | Hyperbolic tangent sigmoid transfer function |
| $pureline(\cdot)$ | Liner transfer function |
| $\vee$ | Maximum operator |
| $o$ | Logic-AND operator |
| $\bullet$ | Logic-OR operator |
| $\beta$ | Regression parameters/coefficients |
| $\overline{I}(\cdot)$ | Upper rough approximation region |
| $\underline{I}(\cdot)$ | Lower rough approximation region |
| $\zeta_{wm}$ | Shape parameter of wavelet |
| $\mu_c$ | Probability of mutation |

| | |
|---|---|
| EEG | Electroencephalogram |
| ECG | Electrocardiographic |
| T1DM | Type 1 Diabetes Mellitus |
| QTc | Corrected QT Interval |
| HR | Heart Rate |
| CGMS | Continuous Glucose Monitoring System |
| VTWNN | Variable Translation Wavelet Neural Network |
| WNN | Wavelet Neural Network |
| FIS | Fuzzy Inference System |
| RBFNN | Radial Basis Function Network |
| FFNN | Flashforward Neural Network |
| WM | Wavelet Mutation |
| PSO | Particle Swarm Optimization |
| GA | Genetic Algorithm |
| BP | Back-propagation Learning |
| HPSOWM | Hybrid Particle Swarm Optimzation |
| HGAPSO | Hybrid PSO with GA mutation |
| ROC | Receiver Operating Characteristic |
| MR | Multiple Regression |
| NLN | Neural-Logic Network |
| BBNN | Block-Based Neural Network |
| BBNN | Block-Based Neural Network |
| R-BBNN | Rough-Block-Based Neural Network |

# Author's Publications

The contents of this thesis are based on the following papers that have been published, accepted, or submitted to peer-reviewed journals and conferences.

**International Journal Papers:**

1. Phyo Phyo San, Sai Ho Ling, and Hung T. Nguyen, "Industrial Application of Evolvable Block-Based Neural Network to Hypoglycemia Monitoring System", *IEEE Transactions on Industrial Electronics*, vol. 60, no, 12, pp. 5892-5901, 2013.

2. Phyo Phyo San, Sai Ho Ling, and Hung T. Nguyen, "Hybrid PSO-based Variable Translation Wavelet Neural Network and Its Application to Hypoglycemia Detection System", *Neural Computing and Applications*, In-press, October, 2012.

3. Sai Ho Ling, Phyo Phyo San and Hung T. Nguyen, "Non-invasive nocturnal hypoglycemia detection for insulin-dependent diabetes mellitus using genetic fuzzy logic method", *International Journal of Computational Intelligence and Applications*, In-press, 2012.

4. Phyo Phyo San, Sai Ho Ling, and Hung T. Nguyen, "Evolvable Rough-Block-Based Neural Network and Its Biomedical Application", *IEEE Transactions on Systems, Man, and Cybernetics B*, Under Revision, July, 2012.

5. Phyo Phyo San, Sai Ho Ling, and Hung T. Nguyen, "Application of Combinational Neural Logic System to Non-Invasive Hypoglycemic Monitor in Patients with T1DM", *IEEE Transactions on Systems, Man, and Cybernetics B*, Under Review, October, 2012.

**International Conference Papers:**

1. Phyo Phyo San, Sai Ho Ling, and Hung T. Nguyen , "Combinational Neural Logic System and Its Industrial Application", *8th IEEE Conference on Industrial Electronics and Applications*, Melbourne, Australia, 19-21 June, pp. 947-952, 2013. (Finalist of IEEE ICIEA 2013 Best Paper Award)

2. Phyo Phyo San, Sai Ho Ling, and Hung T. Nguyen , "Intelligent Detection of Hypoglycemic Episodes in Children with Type 1 Diabetes using Adaptive Neural-Fuzzy Inference System", *34th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, San Diego, California USA, August 28-September 1, pp. 6325-6328, 2012.

3. Phyo Phyo San, Sai Ho Ling, and Hung T. Nguyen , "Optimized Variable Translation Wavelet Neural Network and Its Application in Hypoglycemia Detection

System", *7th IEEE Conference on Industrial Electronics and Applications*, Singapore, 18-20 July, pp. 534-538, 2012.

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5. Phyo Phyo San, Sai Ho Ling, and Hung T. Nguyen , "Block Based Neural Network for Hypoglycemia Detection", *33rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, Boston, USA, August 30-September 3, pp. 5666-5669, 2011.

6. Phyo Phyo San, Sai Ho Ling, and Hung T. Nguyen , "Non-invasive Detection of Hypoglycemic Episodes in Type1 Diabetes Using Intelligent Hybrid Rough Neural System", *35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, Osaka, Japan, July 3-7, Submitted, 2013.

**Chapter in Book:**

1. Sai Ho Ling, Phyo Phyo San and Hung T. Nguyen, "Hypoglycaemia Detection for Insulin-dependent Diabetes Mellitus: Evolved Fuzzy Inference System Approach", *Computational Intelligence and Its Applications: Evolutionary Computation, Fuzzy Logic, Neural Network and Support Vector Machine Techniques*, World Scientific, UK, pp. 61-85, March, 2011.